

Claims

(59)

1. A method for producing mononuclear cells overexpressing IL-10, wherein the method comprises the steps of:
 - (a) providing a composition comprising peripheral blood mononuclear cells (from a mammal);
 - (b) introducing an expression construct comprising a nucleotide sequence encoding a polypeptide having IL-10 activity into at least part of the mononuclear cells; and,
 - (c) recovery of mononuclear cells overexpressing the polypeptide having IL-10 activity, wherein the mononuclear cells overexpressing the polypeptide having IL-10 activity are not specific for a predetermined antigen.
2. A method according to claim 1, wherein composition comprising peripheral blood mononuclear cells is enriched for a subfraction of the peripheral blood mononuclear cells.
3. A method according to claim 2, wherein the subfraction of mononuclear cells is selected from the group consisting of lymphocytes, B cells, T cells, CD4⁺ cells, macrophages, monocytes or dendritic cells (DC).
4. A method according to any one of claims 1 - 3, wherein prior to step (b) the mononuclear cells are proliferated.
5. A method according to claim 4, wherein the mononuclear cells are proliferated in the presence of a proliferating agent.
6. A method according to claim 5, wherein the proliferating agent is at least one of CD3/CD28 or PHA.
7. A method according any one of claim 1 - 6, wherein subsequent to (b) the mononuclear cells are enriched for a subfraction of mononuclear cells.
8. A method according to claim 7, wherein the subfraction of mononuclear cells is selected from the group consisting of lymphocytes, B cells, T cells, CD4⁺ cells, macrophages, monocytes or dendritic cells (DC).

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9. A method according to any one of claims 1 - 8, wherein subsequent to step (b) the mononuclear cells are enriched for cells (over)expressing the IL-10 transgene.
10. A method for producing a pharmaceutical composition comprising mononuclear cells overexpressing IL-10, mixing cells obtained in above claims with suitable pharmaceutical carrier.
11. A composition comprising mononuclear cells containing an IL-10 transgene, wherein the mononuclear cells are not specific for a predetermined antigen.
12. A composition according to claim 11, whereby the composition comprises T cells containing an IL-10 transgene.
13. A composition according to claim 12, whereby the T cells phenotypically mimic regulatory T cells in that the T cells decrease proliferation of autologous responder cells and/or decrease production of the pro-inflammatory cytokine IL-12 by dendritic cells.
14. A composition according to any one of claims 11 - 13, wherein the composition is a pharmaceutical composition comprising in addition to the mononuclear cells a pharmaceutically acceptable carrier.
15. A method of treating a disease associated with undesired activation and/or expansion of T cells, wherein the method comprises administering a pharmaceutical composition according to claim 14 to a subject suffering from a disease associated with undesired activation and/or expansion of T cells.
16. A method according to claim 15, wherein the disease associated with undesired activation and/or expansion of T cells is a Th1-mediated disease, more preferably Th1-mediated inflammatory diseases.
17. A method according to claim 16, wherein the Th1-mediated disease is selected from the group consisting of Crohn's disease, reactive arthritis, insulin-dependent diabetes, colitis, pancreatitis, an lung, an inflammatory eye disease, multiple sclerosis, Hashimoto's thyroiditis,

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Grave's disease, chronic articular reumatism, contact dermatitis, psoriasis, graft rejection, graft versus host disease, and sarcoidosis.

18. A method according to any one of claims 15 - 17, wherein a the composition comprising the mononuclear cells is administered in a therapeutically effective amount.

19. Use of IL-10 overexpressing mononuclear cells as obtained by any of the methods of claims 1 - 9, in the manufacture of a medicament for use in the treatment of disease associated with undesired activation and/or expansion of T cells.